

Correspondence

Ocular toxicity of Anandron

SIR, In studies previously published in 1983 and 1984 on treatment of prostate cancer with the combination of castration and Anandron^{1,2} two of the authors of the paper by Harnois *et al.*³ stressed the 'excellent tolerance and lack of secondary effects other than those related to hypoandrogenicity' of RU 23908 (Anandron). It is therefore surprising to read in 1986 an article by the same authors reporting a high incidence of adverse visual events, investigated in only 18 patients. No indication is given of how these 18 patients were selected among the 97 patients reported on in one of the above-mentioned articles.²

Three placebo-controlled studies of metastatic prostate cancer reported at the Second International Symposium on Cancer of the Prostate (Paris) in June 1986 did not confirm the results of Harnois *et al.* a much lower incidence of visual symptoms was noted (Table 1).

The different percentages obtained in different studies emphasise the need for double-blind placebo controls in the accurate evaluation of the incidence and severity of adverse events. Indeed visual symptoms were reported by 19% of patients in the placebo group of the Canadian study, reflecting either an environmental factor or a different approach to the adverse events questionnaire.

Among 266 patients included in non-comparative and in other double-blind trials and treated with Anandron, 300 mg per day, for periods ranging from a few days to three years (median 12 months) a total of 49 (18%) patients reported delayed dark adaptation. Three of them had to stop treatment because of this symptom. In these patients, as in those who discontinued treatment for other reasons, symptoms disappeared, as noted by Harnois *et al.* Compliance was not decreased because of this symptom, as evidenced by the small percentage of patients who discontinued treatment for this reason, and by the plasma assays of the drug performed after one to 12 months of treatment in 184 patients.⁷

The pathophysiology of this reversible impairment in dark adaptation has not been elucidated yet. It was not correlated with age, concomitant diseases (especially

cardiovascular), or other adverse events, with the exception of alcohol intolerance. The visual symptoms caused by Anandron, which require discontinuation of treatment in 1% of patients, should be weighed against its proved efficacy on metastatic bone pain, performance status, and regression of tumour mass in combination with orchidectomy, as compared with orchidectomy alone.^{4,6}

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SIR, It is clear from the data presented in Table 1 accompanying the letter of Brisset *et al.* that visual symptoms occur in a relatively large proportion of patients with prostate cancer treated with Anandron. In the three studies presented 47 of 153 patients had visual problems,

Table 1 Incidence of visual symptoms in three double-blind placebo-controlled studies with Anandron

		Daily dose of Anandron		
		0 (placebo)	150 mg	300 mg
Brisset <i>et al.</i> (4)	At risk (n)	50	54	54
	Visual symptoms (n;%)	0 (0%)	10 (19%)	15 (28%)
Navratil <i>et al.</i> (5)	At risk (n)	24	-	22
	Visual symptoms (n;%)	0 (0%)	-	3 (14%)
Beland <i>et al.</i> (6)	At risk (n)	75	-	77
	Visual symptoms (n;%)	14 (19%)	-	29 (38%)

thus showing an incidence rate of 30-7%. As mentioned by the authors of that letter, the incidence of side effects depends on the content of the questionnaire and the way the necessary information is collected. In 1982, at the start of our study using Anandron, the visual symptoms noticed in a large proportion of patients were felt to be of low priority, considering the usually serious secondary effects induced by chemotherapy. In fact in the first 60 patients this secondary effect called 'snow-blindness' (or delay in the recovery of vision when going from a light to a dark environment) was reported in 80% of patients, and this information was brought to the attention of the monitor of the Anandron study.

We then realised that any side effect can become a serious problem in the treatment of prostate cancer, where it is imperative to maintain a constant level of antiandrogen in the circulation in order to block the action of androgens at all times. Any lack of compliance or failure to take the drug regularly can cause the development of tumours which will become resistant to the treatment. It is difficult, especially in this category of relatively old patients, to convince all of them of the absolute need always to take the antiandrogen at the prescribed times without any interruption. It is reasonable to assume that any side effect of a drug can become a problem for compliance, especially when the pain and the other symptoms of cancer have disappeared and the patients are back to their normal activity. It is thus extremely tempting for these patients to discontinue taking a drug which has some side effects.

Following this reasoning, we have decided to change to another pure antiandrogen devoid of such visual secondary effects. The 18 patients included in our detailed study recently published¹ were chosen at random among the initial patients treated with Anandron who complained of 'snow-blindness' and were willing to follow the appropriate ophthalmology tests. The photostress recovery time, a photopic test, was higher than normal. As indicated in the letter of Brisset *et al.*, the ocular symptoms disappeared in all cases on cessation of Anandron and change to Flutamid.

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Book reviews

Ocular Therapeutics and Pharmacology. By PHILIP P. ELLIS. Pp. 362. £43.50. Blackwell: Oxford. 1985.

This is a concise book on clinical ocular pharmacology by an American author, and therefore American medications are emphasised. The book is divided into two sections but the

first can be split into two subsections as well. It is entitled ocular therapeutics and covers the clinical pharmacology of common ocular drugs and a large section on the therapy of individual diseases. The second section is entitled therapeutic agents and takes approximately one-third of the book. The text and material are clearly presented.

The first section of the book is basic but practical and well written. It would make an easy source for examination revision, quick reference for unusual drug side effects or treatment of uncommon conditions. The information is generally practical rather than academic, giving, for example, appropriate dosages of subconjunctival antibiotics. A bibliography is given after each chapter but its usefulness is limited by absence of references to it in the text. Perhaps the greatest shortfall of this section (and many other books on ocular pharmacology) is a total lack of data on intra-ocular drug concentrations and pharmacokinetics. Until clinical textbooks contain this type of information ocular pharmacology remains based on clinical experience rather than scientific knowledge. The second section lists most of the usual drugs used in clinical practice and gives their therapeutic data in a similar way to the *British National Formulary*. British readers, however, would find the *BNF* or individual data sheets more useful because these cover drugs more related to British practice but also because they contain more detail.

In summary, this is a book for the clinical ophthalmologist and is perhaps more suited to American than British practice.

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Diagnostic Imaging in Ophthalmology. Eds CARLOS F GONZALEZ, MELVIN H BECKER, JOSEPH C FLANAGAN. Pp. 366. DM 398.00. Springer-Verlag: Berlin. 1986.

This is the work of multiple authorship (31 contributors) which has been written for radiologists, ophthalmologists, neurologists, neurosurgeons, plastic surgeons, and others interested in evaluation of disorders with ophthalmological signs and symptoms. The authors' design is to provide recent knowledge in this subject in ultrasonography, computerised tomography, and nuclear magnetic resonance. There are three sections to the book: the first is a discussion of the imaging techniques; the second is devoted to the role of these imaging methods in the evaluation of ophthalmic disorders; and the last deals with the radiology of ophthalmic tumours.

The book is well produced with excellent illustrations, and it is undoubtedly the most up to date work on the subject. Like most multiple author texts there is some unevenness in the contributions. The section on plain x-ray diagnosis is inadequate, simply consisting of an unqualified list of radiological signs and their known causes without illustrations. On the other hand there is an excellent chapter on the investigation of the orbit by magnetic resonance and an interesting and informative section on computerised tomography in ocular motility disorders. Best of all there is a long chapter on congenital abnormalities which must now be the definitive text on this subject.

The work achieves its objective and is recommended to librarians looking for a textbook on orbital diagnostic imaging. Individual ophthalmologists interested in the subject may find its price excessive.

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